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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,339	03/19/2004	Patricia Cruz-Perez	0001-00001CON1	8012

7590 02/08/2006

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EXAMINER	
WOOLWINE, SAMUEL C	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,339	CRUZ-PEREZ ET AL.	
	Examiner	Art Unit	
	Samuel Woolwine	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 18-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 18-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____. 3/19/2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application has been transferred to Examiner Samuel Woolwine, whose contact information appears below.

Election/Restrictions

The requirement for restriction issued on 12/29/2005 is hereby withdrawn, as the restriction was made over claims which had been cancelled in a preliminary amendment entered on 3/19/2004. The Office regrets any inconvenience caused by this error. Claims 1-17 are cancelled, claims 18-27 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Haugland et al (1999).

With regard to claim 18, Haugland teaches a method comprising:

obtaining a primer set and probe that is specific for the fungal species Stachybotrys chartarum; See page 334, first sentence of *Results*: "The sequences and target sites of the forward (StacF4) and reverse (StacR5) PCR primers and TaqMan

probe (StacP2) constructed for the detection of *S. Chartarum* rDNA sequences in this study are shown in Fig. 1." See also figure 1.

collecting the sample from the environment; See page 333, first sentence of *Collection, recovery and analysis of conidia from air samples*: "Air sampling was performed in rooms that had previously been occupied by infants diagnosed with PH from three homes in the Cleveland, Ohio area."

extracting the sample's DNA; See page 334, last sentence of first paragraph on the page: "Three additional 10µl aliquots of each recovered sample were mixed with *G. candidum* reference conidia and subjected to total genomic DNA extraction for subsequent analysis in the model 7700 as specified above."

obtaining DNA standards from a culture of Stachybotrys chartarum; See page 330, first sentence of second paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Genomic DNAs were extracted from 20µl conidia suspensions using a glass bead milling and glass milk adsorption method."

determining the concentration of Stachybotrys chartarum spores in the DNA standards; See page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

amplifying by polymerase chain reaction each of the DNA standards and the collected sample's DNA using the obtained primer set and probe; See page 332, *PCR amplification and TaqMan analysis in the model 7700*, entire section.

and comparing amplification plots obtained by polymerase chain reaction of each of the DNA standards and the collected sample's DNA to obtain an indication of the presence of the fungus Stachybotrys chartarum in the collected sample and a concentration of the fungus Stachybotrys chartarum in the collected sample. See page 332, last paragraph of *Quantification of S. chartarum conidia using the comparative C_T method*: "Each series of DNA extracts was also analysed using only *S. chartarum* target sequence assay results. In these calculations, calibrator [i.e. standard] sample C_T values were subtracted directly from corresponding test sample C_T values to obtain $\Delta C_{T,STAC}$ values. These values were used in place of $\Delta\Delta C_T$ values to determine the ratio of target sequences in the test and calibrator samples and to quantify *S. chartarum* conidia in the test samples as described above."

With regard to claim 21, *wherein the concentration of Stachybotrys chartarum spores in the DNA standards is determined via direct total count of the Stachybotrys chartarum spores in the DNA standards*, Haugland teaches on page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-20 and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haugland et al (1999) in view of Buck et al (1999) and GenBank ® GI: 3420911.

With regard to claims 19-20 and 22-27, Haugland teaches a method comprising:

obtaining a primer set and probe that is specific for the fungal species Stachybotrys chartarum; See page 334, first sentence of *Results*: "The sequences and target sites of the forward (StacF4) and reverse (StacR5) PCR primers and TaqMan probe (StacP2) constructed for the detection of *S. Chartarum* rDNA sequences in this study are shown in Fig. 1." See also figure 1.

collecting the sample from the environment; See page 333, first sentence of *Collection, recovery and analysis of conidia from air samples*: "Air sampling was performed in rooms that had previously been occupied by infants diagnosed with PH from three homes in the Cleveland, Ohio area."

extracting the sample's DNA; See page 334, last sentence of first paragraph on the page: "Three additional 10µl aliquots of each recovered sample were mixed with *G. candidum* reference conidia and subjected to total genomic DNA extraction for subsequent analysis in the model 7700 as specified above."

obtaining DNA standards from a culture of Stachybotrys chartarum; See page 330, first sentence of second paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Genomic DNAs were extracted from 20µl conidia suspensions using a glass bead milling and glass milk adsorption method."

determining the concentration of Stachybotrys chartarum spores in the DNA standards; See page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in

a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

amplifying by polymerase chain reaction each of the DNA standards and the collected sample's DNA using the obtained primer set and probe; See page 332, *PCR amplification and TaqMan analysis in the model 7700*, entire section.

and comparing amplification plots obtained by polymerase chain reaction of each of the DNA standards and the collected sample's DNA to obtain an indication of the presence of the fungus Stachybotrys chartarum in the collected sample and a concentration of the fungus Stachybotrys chartarum in the collected sample. See page 332, last paragraph of *Quantification of S. chartarum conidia using the comparative C_T method*: "Each series of DNA extracts was also analysed using only *S. chartarum* target sequence assay results. In these calculations, calibrator [i.e. standard] sample C_T values were subtracted directly from corresponding test sample C_T values to obtain $\Delta C_{T,STAC}$ values. These values were used in place of $\Delta\Delta C_T$ values to determine the ratio of target sequences in the test and calibrator samples and to quantify *S. chartarum* conidia in the test samples as described above."

Further, with regard to the limitation *wherein the concentration of Stachybotrys chartarum spores in the DNA standards is determined via direct total count of the Stachybotrys chartarum spores in the DNA standards*, Haugland teaches on page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by

counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

The only limitations of claims 19-20 and 22-27 not taught by Haugland are the specific primers/probes (SEQ ID NOS 1-5) used for the quantification of *Stachybotrys chartarum*. SEQ ID NOS 1-5 were all known sequences of the 18S ribosomal RNA gene of *Stachybotrys chartarum* at the time the invention of the instant application was made as shown by GenBank ® GI: 3420911.

SEQ ID NO 1

```
>gi|3420911|gb|AF081469.1|AF081469  Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene,
partial sequence; internal transcribed spacer 1, 5.8S ribosomal
RNA gene and internal transcribed spacer 2, complete
sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

 Score = 34.2 bits (17),  Expect = 2e-05
 Identities = 17/17 (100%), Gaps = 0/17 (0%)
 Strand=Plus/Plus

Query  1    GTTGCTTCGGCGGGAAC  17
            |||||||||||||||||
Sbjct  405  GTTGCTTCGGCGGGAAC  421
```

SEQ ID NO 2

```
>gi|3420911|gb|AF081469.1|AF081469  Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene,
partial sequence; internal transcribed spacer 1, 5.8S ribosomal
RNA gene and internal transcribed spacer 2, complete
sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

 Score = 40.1 bits (20),  Expect = 5e-07
 Identities = 20/20 (100%), Gaps = 0/20 (0%)
 Strand=Plus/Minus

Query  1    TTTGCGTTTGCCACTCAGAG  20
            ||||||||||||||||||||
Sbjct  511  TTTGCGTTTGCCACTCAGAG  492
```

SEQ ID NO 3

```
>gi|3420911|gb|AF081469.1|AF081469  Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene,
partial sequence; internal transcribed spacer 1, 5.8S ribosomal
RNA gene and internal transcribed spacer 2, complete
sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

 Score = 38.2 bits (19),  Expect = 2e-06
 Identities = 19/19 (100%), Gaps = 0/19 (0%)
 Strand=Plus/Plus

Query  1    ACCTATCGTTGCTTCGGCG  19
            ||||||||||||||||||
Sbjct  398  ACCTATCGTTGCTTCGGCG  416
```

SEQ ID NO 4

```
>gi|3420911|gb|AF081469.1|AF081469  Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene,
partial sequence; internal transcribed spacer 1, 5.8S ribosomal
RNA gene and internal transcribed spacer 2, complete
sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

 Score = 46.1 bits (23),  Expect = 1e-08
 Identities = 23/23 (100%), Gaps = 0/23 (0%)
 Strand=Plus/Minus

Query  1    GCGTTTGCCACTCAGAGAATACT  23
            |||||||||||||||||||||||
Sbjct  508  GCGTTTGCCACTCAGAGAATACT  486
```

SEQ ID NO 5

```
>gi|3420911|gb|AF081469.1|AF081469  Stachybotrys chartarum strain UAMH 7900 18S ribosomal RNA gene,
partial sequence; internal transcribed spacer 1, 5.8S ribosomal
RNA gene and internal transcribed spacer 2, complete
sequence; and 28S ribosomal RNA gene, partial sequence
Length=936

 Score = 36.2 bits (18),  Expect = 7e-06
 Identities = 18/18 (100%), Gaps = 0/18 (0%)
 Strand=Plus/Plus

Query  1    CTGCGCCCGGATCCAGGC  18
            ||||||||||||||||||
Sbjct  433  CTGCGCCCGGATCCAGGC  450
```

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties"

Since the claimed primers/probes simply represent functional homologues of the primers/probes taught by Haugland, the claimed primers/probes are *prima facie* obvious over Haugland's primers/probes in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2 and 17 of U.S. Patent No. 6,733,999 in view of Haugland et al (1999).

With regard to claims 18 and 21, claims 2 and 17 of the '999 patent teach a method of detecting the fungus *Stachybotrys chartarum* using specific probes and primers. Claims 18 and 21 in the instant application are generic with respect to the primers and probes used for identifying and quantifying the fungus and are thereby rendered obvious in this respect by claims 2 and 17 of the '999 patent. Claims 2 and 17 of the '999 patent do not teach the steps of preparing DNA standards from a culture of spores to allow quantification of *Stachybotrys chartarum* in the test sample. Haugland

et al teach all of the limitations of claims 18 and 21 as stated in the rejection of claims 18 and 21 under 35 U.S.C. 102 above, including the use of DNA standards prepared from spores to quantify *Stachybotrys chartarum* in the test sample (see page 330, *Fungal cultures, conidia stocks and genomic DNA extraction*) and the direct counting of spores in the DNA standards (see page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*). It would have been obvious to one of ordinary skill in the art at the time the invention of the instant application was made to apply the use of DNA standards as taught by Haugland to the methods of claims 2 and 17 of the '999 patent. One would have been so motivated because this would allow for the accurate quantitation of *Stachybotrys chartarum* in the test sample instead of merely the detection of the fungus.

With regard to claims 19, 20, and 22-27 which recite the use of specific primers and probes for the quantification of *Stachybotrys chartarum* in the test sample, claims 2 and 17 of the '999 patent teach the same primers and probes.

With regard to claims 21, 24 and 27, which recite the additional limitation of determining the concentration of *Stachybotrys chartarum* spores in the standards by direct total counts, Haugland teaches on page 330, fourth sentence of first paragraph under *Fungal cultures, conidia stocks and genomic DNA extraction*: "Cell concentrations in these stock suspensions were determined by counting under a microscope at 400× magnification in a haemocytometer chamber, after which the suspensions were divided into ~200µl aliquots for storage at -80°C."

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Woolwine whose telephone number is (571) 272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

scw

JEFFREY FREDMAN
PRIMARY EXAMINER
2/3/06

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